Environmental Research Section A 80, 222–230 (1999)
Article ID enrs.1998.3895, available online at http://www.idealibrary.com on IDEAL®

Variation in Blood Concentrations of Cadmium and Lead in the Elderly

Maria Bæcklund,* Nancy L. Pedersen,*,† Lars Björkman,*,‡ and Marie Vahter*

*Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; †Department of Psychology, University of Southern California, Los Angeles, California 90089; ‡Department of Basic Oral Science, Karolinska Institutet, Stockholm, Sweden

Received January 20, 1998

This study aims at characterizing blood concentrations of cadmium (B-Cd) and lead (B-Pb) in a group of 176 men and 248 women, 49–92 years of age (mean 68 years), selected from the Swedish Twin Registry. Metal concentrations were determined using graphite furnace atomic absorption spectrophotometry. B-Cd ranged from 0.05 to 6.8 μg Cd/L (median 0.36 μg Cd/L) and B-Pb from 5.6 to 150 μg Pb/L (median 27 μg Pb/L). As expected, smokers had higher B-Cd than nonsmokers (median 1.3 versus 0.32 μg Cd/L), while B-Pb was not significantly related to smoking habits. Among nonsmokers, women had higher B-Cd than men (median 0.35 versus 0.25 μg Cd/L). In men, but not women, B-Cd increased with age and consequently the gender-related difference in B-Cd was most obvious in the youngest age group. On the other hand, women had lower B-Pb than men (median 24 versus 30 μg Pb/L). In both men and women, B-Pb decreased between 50 and 70 years of age, perhaps reflecting decreased energy intake. In women, the highest B-Pb in the 50–55 years age group is probably related to an increased release of Pb from the skeleton during postmenopausal bone demineralization. After about 70 years, B-Pb tended to increase, which probably is a cohort effect due to much higher Pb exposure 10–30 years ago when leaded gasoline was used. © 1999 Academic Press

Key Words: **cadmium; lead; aging; gender; smoking habits; occupational exposure.**

INTRODUCTION

Both cadmium (Cd) and lead (Pb) accumulate in the human body with long biological half-lives, causing continuous increase in target tissue concentrations (for review, see WHO, 1992, 1995). The half-lives of Cd in the kidneys and Pb in bone are on the order of decades (Nordberg and Nordberg, 1988; WHO, 1992; Nilsson and Skerfving, 1993; Skerfving *et al.*, 1993). There is increasing evidence that the long-term tissue accumulation of metals eventually may lead to tissue damage even in the case of low-dose exposure in the general population (Skerfving, 1993; Järup *et al.*, 1998). For example, autopsy data have shown that Cd concentration in the kidneys increases with age to 50–60 years of age, after which it decreases, probably as a result of kidney damage (Elinder *et al.*, 1976; Vahter, 1982, Friis *et al.*, 1998). In addition, tissue metal accumulations may serve as significant sources of endogenous exposure (Silbergeld *et al.*, 1988). Concentrations of Cd and Pb in blood (B-Cd, B-Pb) mainly reflect recent exposure, but are also influenced by the body burden, especially after long exposure (Skerfving *et al.*, 1993; Berglund *et al.*, 1994; Järup *et al.*, 1997).

In spite of the very long biological half-lives of Cd and Pb, and the narrow safety margins between the current tissue concentrations and the concentrations at which toxic effects are seen, there are very few data on exposure levels of these metals in elderly people. Aging is associated with major changes in body constitution and physiological functions, most of which may influence the kinetics and toxic effects of xenobiotics, e.g., toxic metals. Starting already at about 35 years of age, bone mass decreases by about 0.5–1% a year, somewhat more in women than in men (Matkovic, 1992). After menopause, there is a dramatic increase in bone demineralization in women, as much as 3–6% of the total bone mass a year, or about 25% in 4–10 years. Other changes in elderly people include increase in body fat, and decrease in body water and plasma volume, as well as changes in absorption and metabolism. Exposure to toxic metals may reduce the reserve capacity of the human body (Grandjean, 1995), but the effects of life-long metal exposure on aging people seem not to have been investigated. The aim of this study was to determine B-Cd and B-Pb in relation to age, gender,

0013-9351/99 $30.00

and previous occupational exposure in elderly people. In addition, the association between blood metal concentrations and cognitive function was studied.

METHODS

This study was carried out within The Swedish Adoption/Twin Study of Aging (SATSA), a longitudinal research project in gerontological genetics based on a subsample of twins from the Swedish Twin Registry. The SATSA cohort consists of twins, 50 years of age and older, reared apart and a sample of twins reared together, matched by gender, age, and county of birth (Pedersen *et al.*, 1984, 1991). The SATSA project includes in-person testing sessions at 3-year intervals. At each testing session, individuals with dementia, and their cotwins, were transferred to another cohort, and thus not present in this project. During the third interpersonal testing session (IPT-3, which included 569 individuals and was carried out between 1992 and 1994), blood samples collected by specially trained nurses were made available for metal analyses. Details on the testing procedures have been described elsewhere (Pedersen *et al.*, 1991).

Questions about former and current occupations were included both in a mailed questionnaire and in a structured interview. All occupations were classified according to the International Standard Classification of Occupations codes (ISCO codes). Possible occupational exposure to cadmium and lead was assessed in collaboration with the Department of Occupational Medicine at the Karolinska Hospital and by using information from previous publications (Nordin, 1943; Skerfving, 1993; Stenlund, 1996). Individuals having an occupation associated with exposure to Cd or Pb for more than 1 year were classified as occupationally exposed to the metal. In Table 1, the occupations considered to be associated with exposure to Cd and Pb are given.

Questions on smoking status were included in the mailed questionnaire. Individuals who had not smoked within the last 3 years were designated as nonsmokers. Former smokers were individuals who had stopped smoking more than 1 month but less than 3 years ago, and current smokers were present smokers. The distribution of smoking habits and occupational exposure by age and gender is given in Table 2.

Within SATSA, psychometric tests relevant for assessment of age-related changes in cognitive abilities were included. Mini-Mental State Examination (MMSE, Folstein *et al.*, 1975) was used as a screening instrument for dementia. Memory-related tests included Digit Span Forward and Backward, Names and Faces Immediate and Delayed, and Thurstone's Picture Memory (Pedersen *et al.*, 1992).

TABLE 1
Occupations Assessed to be Associated with a Risk of Potential Exposure to Cadmium and Lead

Cadmium[a]	Lead[b]
Alloy production	Lead smelting, refining
Cable and trolley wire makers	Paint production
Cadmium plating	Paint spraying with lead color
Ceramics pottery making	Soldering, tinning
Copper–cadmium alloy making	Ship-breaking
Battery production	Lead sanding, grinding
Glass making	Wire patenting
Pigment production and use	Bronze pouring
Smelting and refining	Battery production
Soldering	Repair of automobile radiators
Welding, cadmium alloy	Printing
Welding, cadmium-plated objects	Lead sawing
Plastics production	Lead-glass working
Zinc mining, smelting, and refining workers	Petrol-tank cleaner
	PVC manufacturing (Pb stabilizes PVC).

[a]Adapted from Zenz (1988) and WHO (1992).
[b]Adapted from Skerfving (1993), Nordin (1943), and WHO (1995).

Samples of venous blood (2 × 10 ml) were collected from the cubital vein using Vacutainer tubes containing K_3EDTA (Becton Dickinson, England). Each blood sample was transferred to polypropylene tubes and frozen at −80°C. The sampling material was tested and found free from contamination by Cd and Pb. All the nurses were nonsmokers, which is essential for eliminating a potential risk of contamination of the samples, especially by Cd. Blood for metal analysis was available for 424 of a total of 569 individuals. The total age range was 49–92 years, with a mean of 68 years. There were no significant differences in age and gender distribution between the 424 individuals (176 men, mean age 67 years, SD 8 and 248 women, mean age 70 years, SD 9) with blood samples available for metal analysis and the 145 individuals with insufficient sample quantities.

The concentrations of Cd and Pb in whole blood (B-Cd and B-Pb) were determined by graphite furnace atomic absorption spectrophotometry (GFAAS, Perkin Elmer 5000 AAS with Zeeman background correction and graphite furnace HGA-500 with L'vov platform). Aliquots of whole blood (0.3 ml) were analyzed in duplicate for Cd and Pb after deproteinization by addition of 0.8 M HNO_3 (0.5 ml, Suprapur,

TABLE 2

Smoking Habits and Occupational Exposure to Cadmium and Lead by Age and Gender

	Men		Women		Total	
	≤ 65 years	>65 years	≤ 65 years	>65 years	≤ 65 years	>65 years
Smoking habits[a]						
Nonsmoker	45 (11%)	80 (19%)	52 (12%)	153 (36%)	97 (23%)	233 (55%)
Former smoker	6 (1%)	5 (1%)	4 (1%)	8 (2%)	10 (2%)	13 (3%)
Current smoker	19 (4%)	20 (5%)	18 (4%)	10 (2%)	37 (9%)	30 (7%)
Occupational exposure[b]						
Cadmium	27 (6%)	36 (8%)	2 (0.5%)	9 (2%)	29 (7%)	45 (11%)
Lead	28 (7%)	53 (12%)	2 (0.5%)	9 (2%)	30 (7%)	62 (15%)

Note. Number (and percentage) of individuals for the included individuals ($n = 424$) are given.

[a]Data on smoking habits were not available for four individuals.

[b]For 16 and 21 individuals, it was not possible to make an assessment of previous occupational exposure to cadmium and lead, respectively.

Merck, Germany) according to the method of Stoeppler and Brandt (1978, 1980). In 16 analytical runs the average detection limit (mean of blank +3 SD) was 0.05 μg/L (range 0.03–0.12 μg/L) for Cd and 1.7 μg/L (range 0.93–3.6 μg/L) for Pb. The limit of quantitation (LOQ = mean of blank + 10 SD) for the Cd analyses was 0.16 μg/L and 5.6 μg/L for the analyses of Pb. Of the analyzed samples, 8.5% were below LOQ for the Cd analyses and none was below LOQ for the Pb.

Analytical performance was evaluated by analyses of sets of quality control (QC) samples, consisting of bovine blood spiked with known amounts of the Cd and Pb (Lind *et al.*, 1988). The results (y) were evaluated against the reference values (x) by linear regression analysis (Vahter, 1982; Friberg and Vahter, 1983). The regression line, based on 17 sets of 6 QC samples, was $y = 0.98x - 0.031$ ($R^2 = 0.998$) for Cd, while that for Pb was $y = 1.00x + 1.39$ ($R^2 = 0.996$). In addition, two external reference control samples (Seronorm Trace Elements, Whole Blood No. 205052, No. 203056, Nycomed Pharma Norway) were analyzed for Cd and Pb. Results from the analysis for Cd were 0.9 and 6.4 μg Cd/L (reference value 0.9, range 0.8–1.0 μg Cd/L, and 6.4, range 5.9–6.8 μg Cd/L). For Pb, the results were 31 and 388 μg Pb/L (reference values 35, range 31–41 μg Pb/L, and 383, range 361–396 μg Pb/L).

Hemoglobin concentration in blood was measured by a photometric test method (AB LEO Diagnostica, 1985, Malmö, Sweden).

Statistical Analysis

Variables with a skewed distribution (B-Cd, B-Pb) were log transformed ($\log_{10}$) to achieve normal distribution. To compare blood concentrations of Cd or Pb between groups, Student's t test or Mann–Whitney U test was used. Linear regression and GLM were used to test the effects of age, gender, and occupational exposure to cadmium and lead, and smoking status and other potential covariates on B-Cd and B-Pb. The statistical analyses were performed using SPSS for Windows (SPSS Inc., Chicago, IL). P values <0.05 were considered as significant.

This study was approved by the ethics committee of Karolinska Institute and the Swedish National Data Inspection Authority.

RESULTS

Cadmium

Factors influencing B-Cd were investigated by GLM, using log B-Cd as the dependent variable. Gender, smoking, and occupational exposure to Cd were included as factors, and age was included as covariate. Cadmium in blood was affected by smoking and gender ($P < 0.001$, Table 3). On average, smokers had 4–5 times higher B-Cd than nonsmokers (Table 4). Among nonsmokers, women had a significantly higher B-Cd than men, especially in the youngest age groups ($P < 0.001$, Tables 4 and 5). Regression analyses with only nonsmokers indicated that log B-Cd increased significantly with age in men ($R^2 = 0.044$, $\beta_{age} = 0.0065$, $n = 125$, $P = 0.019$), but not in women (Fig. 1). Non smoking men with present or previous occupations that possibly involved exposure to Cd had slightly higher B-Cd than those with other occupations (median 0.31 versus 0.23 μg/L, $P = 0.059$). A linear model for nonsmoking men including age and occupational exposure to Cd indicated that occupationally exposed men had on

TABLE 3

GLM Analyses of Potential Predictor Variables for Cadmium in Blood (log_{10} [μg Cd/L blood]) for Individuals with Valid Data for the Included Covariates

	Parameter estimates			
Parameter	B	Std. error	*t*	*p*
Intercept	0.120	0.103	1.164	0.245
Gender[a]	−0.106	0.027	−3.927	0.000
Nonsmoker[b]	−0.655	0.034	−19.387	0.000
Former smoker[b]	−0.425	0.058	−7.292	0.000
No occupational exp.[c]	−4.5E-02	0.034	−1.331	0.184
Age (years)[d]	1.43E-03	0.001	1.021	0.308

Note. $r = 405$. The adjusted R^2 was 0.493.
[a]Reference category: Female gender.
[b]Reference category: Current smoker.
[c]Reference category: Occupational exposed.
[d]Continuous variable.

average 0.07 μg Cd/L higher B-Cd at 65 years of age. A similar tendency was seen for women, however, there were very few occupationally exposed women, and the difference was not significant. When the nonsmoking men were divided into groups below and above 65 years of age (the age of retirement in Sweden), the influence of occupational exposure on B-Cd was more pronounced in the older age group (median, 0.45 versus 0.24 μg Cd/L, $P = 0.018$) than in the younger group (median 0.25 versus 0.22 μg Cd/L, $P > 0.05$).

Lead

Analyses using log B-Pb as the dependent variable and gender, occupational exposure to Pb, and smoking as explanatory factors, and concentration of blood hemoglobin, age, and age squared as covariates, showed that men had higher B-Pb than women ($P < 0.001$, Tables 5–7, Fig. 2). Both age and age squared at the same time were significant covariates for B-Pb ($P = 0.003$ and $P = 0.004$, respectively). This indicates that there was both a linear (age) and a nonlinear (age squared) relationship with age. This effect was significant also when analyses were

TABLE 4

Concentrations of Cadmium in Blood (μg Cd/L) by Gender and Smoking Status

Smoking status	Men	Women	Total
Nonsmokers			
Median	0.25	0.35	0.32
Range	0.05–2.2	0.11–1.1	0.05–2.2
10–90 percentile	0.13–0.6	0.18–0.57	0.15–0.56
n	125	205	330
Former smokers			
Median	0.44	0.46	0.44
Range	0.29–0.82	0.25–1.6	0.25–1.6
10–90 percentile	0.29–0.80	0.26–1.6	0.26–1.3
n	11	12	23
Current smokers			
Median	1.3	1.4	1.3
Range	0.11–6.8	0.21–5.6	0.11–6.8
10–90 percentile	0.51–3.4	0.75–3.1	0.58–3.0
n	39	28	67
Total			
Median	0.32	0.36	0.36
Range	0.05–6.8	0.11–5.6	0.05–6.8
10–90 percentile	0.14–1.5	0.20–0.91	0.17–1.3
n	176	248	424

Note. Median value, range, 10 and 90 percentiles are given.

TABLE 5

Median, 10- and 90 percentiles for Concentrations of Cadmium and Lead in Blood by Age

		Cadmium (μg Cd/L)			Lead (μg Pb/L)		
Gender	Age group	*n*	Median	10–90 percentiles	*n*	Median	10–90 percentiles
Men	< 55	11	0.17	0.09–0.36	19	33	19–68
	55–64	34	0.25	0.13–0.55	51	38	20–62
	65–74	64	0.24	0.14–0.61	85	28	15–61
	75–84	15	0.31	0.12–0.67	20	35	19–70
	> 85	1	0.32	—	1	40	—
Women	< 55	11	0.41	0.23–0.67	19	28	19–62
	55–64	41	0.35	0.15–0.54	55	26	14–44
	65–74	83	0.34	0.19–0.59	92	24	14–38
	75–84	61	0.35	0.17–0.61	72	25	12–50
	> 85	9	0.35	0.18–0.47	10	22	14–86

Note. For cadmium, only data for nonsmokers are given.

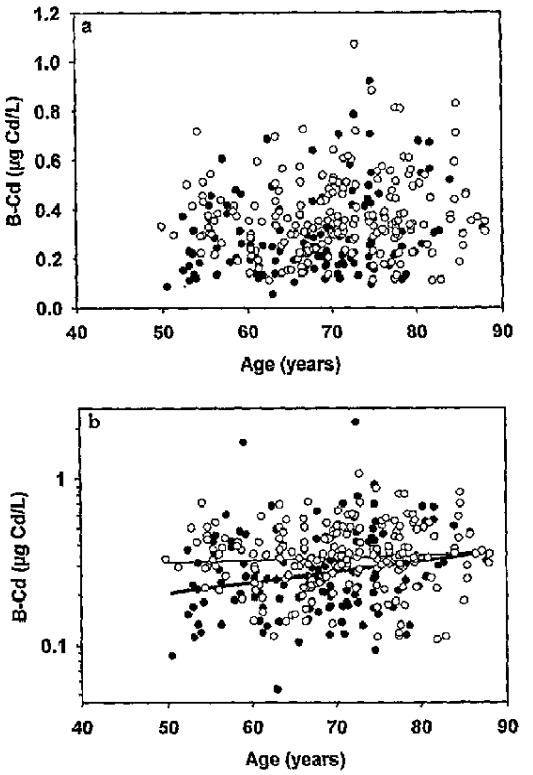

FIG. 1. Cadmium concentrations in blood in nonsmoking men (●) and women (○) in relation to age. In panel *a*, cadmium concentrations are given as micrograms Cd/L. The two highest observations (with B-Cd of 2.2 and 1.7 µg/L, both men) were excluded from the graph. In panel *b*, the concentrations are given on a $\log_{10}$ scale and the regression lines for men (——, $P = 0.02$, $n = 125$) and women (– – –, $P = 0.34$, $n = 205$) are shown.

made for men and women separately (see Fig. 2b). In both men and women under 70 years, B-Pb decreased across age ($r^2 = 0.05$, $\beta_{age} = -0.0075$, $P = 0.02$ and $r^2 = 0.06$, $\beta_{age} = -0.0079$, $P = 0.01$). After 70 years of age, B-Pb increased again. In Table 5 the median and 10 and 90 percentiles for B-Pb are given by gender and age. There were four women older than 70 years with relatively high levels of Pb and the variance was four times higher for women older than 70 years old compared to younger women (525 versus 120). There was a tendency toward higher B-Pb in smokers than in nonsmokers, both in men and women, but the differences were not significant (Tables 6 and 7). About 48% of the nonsmoking men had been working in occupations with possible exposure to Pb, compared to only about 3% of the women. Individuals with a possible occupational exposure to Pb did not have higher B-Pb than those not occupationally exposed. When occupationally exposed men were analyzed in a separate model, both

TABLE 6

GLM Analyses of Potential Predictor Variables for Lead in Blood ($\log_{10}$ [µg Pb/L blood]) for Individuals with Valid Data for the Included Covariates

	Parameter estimates			
Parameter	B	Std. error	*t*	*p*
Intercept	2.961	0.561	5.278	0.000
Gender[a]	0.124	0.028	4.511	0.000
Nonsmoker[b]	−4.6E-02	0.029	−1.561	0.119
Former smoker[b]	−7.9E-02	0.050	−1.583	0.114
No occupational exposure[c]	4.01E-02	0.029	1.390	0.165
Age (years)[d]	−4.8E-02	0.016	−2.981	0.003
Age squared (years²)[d]	3.49E-04	0.000	2.924	0.004
Hemoglobin (g Hb/L)[d]	6.40E-04	0.001	0.653	0.514

Note. $n = 394$. The adjusted R^2 was 0.094.
[a]Reference category: Female gender.
[b]Reference category: Current smoker.
[c]Reference category: Occupational exposed.
[d]Continuous variable.

TABLE 7

Concentrations of Lead in Blood (µg Pb/L) by Gender and Smoking Status

Smoking status	Men	Women	Total
Nonsmoker			
Median	30	24	26
Range	11–104	6.0–140	6.0–140
10–90 percentile	18–57	14–43	14–49
n	125	205	330
Former smoker			
Median	26	26	26
Range	13–50	8.5–66	8.5–66
10–90 percentile	14–49	9.8–61	13–51
n	11	12	23
Current smoker			
Median	34	28	31
Range	16–107	11–62	11–107
10–90 percentile	19–72	16–43	18–63
n	39	28	67
Total			
Median	31	25	27
Range	11–110	5.6–150	5.6–150
10–90 percentile	17–60	14–43	15–53
n	176	248	424

Note. Median value, range, and 10 and 90 percentiles are given.

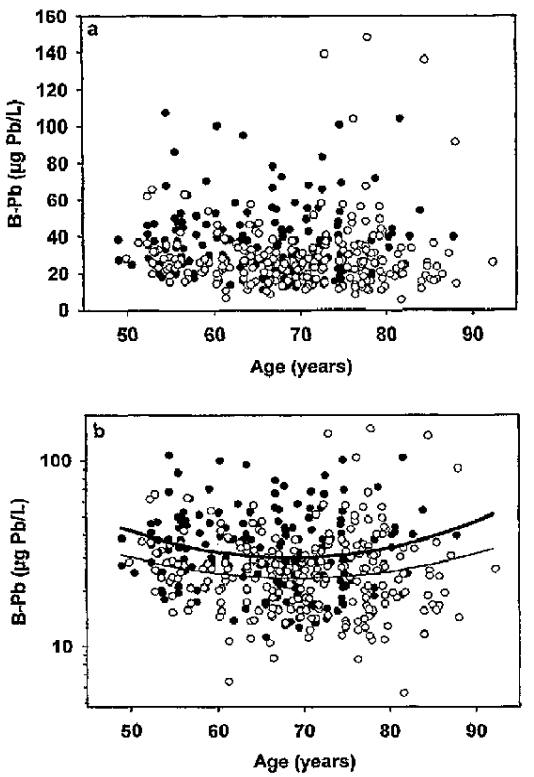

FIG. 2. Lead concentrations in blood in men (•) and women (○) in relation to age. In panel *a*, lead concentrations are given as micrograms Pb/L, and in panel *b*, the concentrations are given on a $\log_{10}$ scale and the regression lines (adjusted for smoking habits, occupational exposure to Pb, and hemoglobin concentration in blood) for nonsmoking men (——) and women (——) without occupational exposure and with an average hemoglobin concentration in blood (144 g/L for men and 131 g/L for women) are shown. The *P* values for age and age squared were 0.04 and 0.05 for men and 0.04 and 0.04 for women, respectively.

age and age squared showed slightly stronger effects ($\beta_{age} = -0.106$, $P = 0.02$ and $\beta_{age\ squared} = 0.00081$, $P = 0.02$) compared to the average effects for the entire group (Table 7). Because occupational exposure to Pb was a rare event in women, the effect on B-Pb was not possible to evaluate.

There were no significant correlations between B-Cd and any of the measures of cognitive function. There were positive significant correlations between B-Pb and scores of the digit span forward and MMSE test. However, after controlling for age, gender, and education, no significant associations between cognitive function and B-Pb were found.

DISCUSSION

This study indicates that nonsmoking women have significantly higher B-Cd than nonsmoking men, and, in contrast to the men, there is no increase in B-Cd with age above 50 years of age. The gender-related difference in B-Cd is probably related to an elevated intestinal absorption of dietary Cd in women with low body iron stores. Previous studies have shown that 10–40% of premenopausal women in Sweden have empty iron stores (Rybo, 1985; Berglund *et al.*, 1994), and that this is associated with elevated B-Cd (Berglund *et al.*, 1994). In the latter study, B-Cd in nonsmoking women increased with age from 0.24 µg/L at 38 years to about 0.40 µg/L at 50 years of age. The present study is consistent with this finding; women 49–55 years of age had a median of 0.41 µg/L. Thus, there is a significant increase in B-Cd with age in women until the time of menopause. After menopause, when there is no more monthly loss of iron, the increased iron stores most likely results in a lower absorption of dietary Cd, counteracting the increase in B-Cd as a function of increasing body burden. A higher uptake of Cd in women is also indicated by findings of higher kidney cadmium concentrations than in men (Elinder *et al.*, 1986; Friis *et al.*, 1998). Recent studies also indicate that Cd exposure may be one out of several risk factors for osteoporosis, one of the major public health problems, especially among women. Cd-induced kidney damage alters the vitamin D-dependent regulation of calcium, which may lead to loss of calcium and disturbed bone mineralization (Goyer *et al.*, 1994; Järup *et al.*, 1998). It has been reported that the urinary excretion of Cd in the general population is positively associated with urinary excretion of calcium (Staessen *et al.*, 1992, Staessen and Lauwerys, 1993), and negatively associated with bone density (Tsuritani *et al.*, 1996). Also against this background it is disturbing that women in Sweden continue to smoke. In this study, smokers had 4–5 times higher B-Cd than nonsmokers. Thus, smoking women with low iron stores seem to be the main risk group for cadmium exposure (Järup *et al.*, 1998).

There were slightly higher B-Cd concentrations in individuals with previous occupational exposure, especially in men above 65 years of age. This may be related to the fact that occupational exposure to Cd has decreased considerably during the past decades as a result of occupational regulations. Because Cd has a long biological half-life in the body, people will have a higher body burden of Cd and higher B-Cd many years after the cessation of exposure (Järup *et al.*, 1997).

Average B-Pb was about 25% lower than that reported for non-Hispanic whites in the United States (Brody *et al.*, 1994), most likely reflecting a lower exposure to lead in Sweden. One reason is the fact that lead-based paint has rarely been used in Sweden. The present average B-Pb level was about 50% lower than that reported for elderly people (age range 56–72 years) in Sweden 15 years ago (Elinder *et al.*, 1983). This decrease in B-Pb is mainly associated with the decreased use of leaded gasoline (Elinder *et al.*, 1986; Vahter *et al.*, 1991; Strömberg *et al.*, 1995). There was a wide range in B-Pb in all age groups (5–150 μg Pb/L), which partly may be explained by variations in dietary habits. Studies on concentrations of Pb in duplicate diets collected during 7 consecutive days by 15 women showed a total range of 5 to 80 μg Pb per day (Vahter *et al.*, 1991). Elevated lead levels may be found; e.g., in canned food and wine (Jorhem *et al.*, 1988; Jorhem and Sundström, 1993). However, there may also be variations in the sources of exposure. For example, it has been reported that rifle shooting (Svensson *et al.*, 1992) and automobile repair (Nunez *et al.*, 1993) may cause a significant increase in B-Pb. Further, there may be interindividual variations in the kinetics of Pb (Skerfving *et al.*, 1993), which may be genetically determined.

In accordance with previous studies (Vahter, 1982), women had lower B-Pb than men. More than 95% of B-Pb is localized in the erythrocytes and in general B-Pb is associated with the hematocrit (Hense *et al.*, 1992). Thus, the higher B-Pb in men may to some extent be explained by their higher hematocrit compared to that in women. Hematocrit was not measured in the present study, but there was no significant association between B-Pb and Hb, which is closely correlated with hematocrit. Although the gender-related difference in B-Pb decreased somewhat when B-Pb was adjusted for Hb, men still had higher B-Pb than women (30 versus 25 μg Pb/L). Probably, the main gender-related difference in B-Pb may be explained by higher exposure to Pb in men due to, for example, occupational exposure and lifestyle habits (see above). Forty-nine percent of all men, but only 3% of the women, had been working in occupations with a potential risk of exposure to lead. Although, the results from the multivariate analysis (Table 7) showed no evidence of elevated B-Pb in individuals with possible occupational exposure, the effect of age on B-Pb was more pronounced in those men. This may be related to the methodological problems associated with this kind of retrospective occupational exposure assessment.

Contrary to the case with B-Cd, the change in B-Pb with age was quite similar in women and men. For both men and women, there was a slow decline in B-Pb with increasing age up to 70 years of age, after which there seemed to be an increase. As the diet is the major source of Pb exposure, the decrease in energy intake after about 50 years of age (Becker, 1994) related to a decrease in basal metabolic rate (Passmore and Eastwood, 1986) is likely to result in a decreased dietary intake of Pb. In women, the highest B-Pb was found below 55 years of age, which may be related to a peak in mobilization of Pb from the skeleton associated with the postmenopausal increase in bone demineralization. More than 90% of the total body burden of Pb is stored in the skeleton, and a significant increase in B-Pb after menopause has been observed among American women (Silbergeld *et al.*, 1988). An age-related decrease in bone Pb has also been observed in experimental animals exposed via drinking water, along with an increase in brain Pb levels (Cory-Slechta, 1990). In on-going studies on dietary lead exposure in Swedish women 20–50 years of age, the average B-Pb was 24 μg/L (Vahter, unpublished data), i.e., similar to that in the oldest women in the present study.

The multivariate model gave evidence for an age-related increase in B-Pb after about 70 years of age (Fig. 2). This increase was not dependent on the few observations with the highest B-Pb (> 100 μg/L), and the effect remained after exclusion of these individuals in the analyses (data not shown).The age-related increase in B-Pb may be explained by a cohort effect related to the change over time in exposure. As mentioned above, the exposure to lead from gasoline was considerably higher in the 1970s than today, resulting in a much higher incorporation of Pb in the skeleton during the continuous remodeling of the bone (about 10% a year; Teitelbaum, 1993). In men, the high B-Pb in the oldest age groups was especially marked in those previously occupationally exposed. This may be related to mobilization of bone lead in connection with the demineralization of the skeleton, which occurs later in life in men than in women.

There were no significant associations between cognitive functions and B-Pb after controlling for age, gender, and education. However, twins with dementia were not included in this study. Muldoon *et al.* (1996) examined women over 65 years of age, and observed that B-Pb exceeding 80 μg Pb/L was associated with poorer cognitive functions, as measured by neuropsychological tests. In the present study, there were only five women with B-Pb > 80 μg/L. There are also studies showing negative

associations between cognitive functions and occupational exposure to lead (Hänninen *et al.*, 1978). However, the occupational exposure was high, resulting in a blood concentration of more than 400 μg Pb/L, compared to 27 μg Pb/L in the present study.

The blood metal concentrations observed in the present study are fairly low, but there is considerable interindividual variation. Although these exposure levels have not been proven to cause serious adverse health effects, they may exert extra stress on aging tissues and may contribute to premature aging (Grandjean, 1991). Understanding the biological basis of the interactions between toxic metals and the aging process is a major scientific challenge that will require integration of medical, genetic, and toxicological approaches.

ACKNOWLEDGMENTS

Technical assistance by Bo Nilsson, Pia Svedberg, Inger Isaksson, and Gun Nise is gratefully acknowledged. The Swedish Adoption Twin Study of Aging was supported by the National Institute on Aging (Grants AG-04563 and AG-10175), the MacArthur Foundation Research Network on Successful Aging, and the Swedish Council for Social Research. In addition, support for this study has been provided by the Swedish Environmental Protection Agency.

REFERENCES

Becker, W. (1994). "Food Habits and Nutrient Intake in Sweden 1989". *National Food Administration, Uppsala, Sweden.*

Berglund, M., Åkesson, A., Nermell, B., and Vahter, M. (1994). Intestinal absorption of dietary cadmium in women depends on body iron stores and fiber intake. *Environ. Health Perspect.* **102,** 1058–1066.

Brody, D. J., Pirkle, J. L., Kramer, R. A., Flegal, K. M., Matte, T. D., Gunter, E. W., and Paschal, D. C. (1994). Blood lead levels in the US population. Phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991). *J. Am. Med. Assoc.,* **272,** 277–283.

Corey-Slechta, D. A. (1990). Lead exposure during advanced age: Alterations in kinetics and biochemical effects. *Toxicol. Appl. Pharmacol.* **104,** 67–78.

Elinder, C.-G., Lind, B., Kjellström, T., Linnman, L., and Friberg, L. (1976). Cadmium in kidney cortex, liver and pancreas from Swedish autopsies. Estimation of biological half time in kidney cortex, considering calorie intake and smoking habits. *Arch. Environ. Health* **31,** 292–302.

Elinder, C.-G., Friberg, L., Lind, B., and Jawaid, M. (1983). Lead and cadmium levels in blood samples from the general population of Sweden. *Environ. Res.* **30,** 233–253.

Elinder, C.-G., Friberg, L., Lind, B., Nilsson, B., Svartengren, M., and Övermark, I. (1986). Decreased blood lead levels in residents of Stockholm for the period 1980–1984. *Scand. Work J. Environ. Health* **12,** 114–120.

Folstein, M. F., Folstein, S. E., and McHugh, P. R. (1975). Mini-Mental State; A practical method for grading the cognitive state of patients for the clinician. *J. Psychiat. Res.* **12,** 189–198.

Friberg, L., and Vahter, M. (1983). Assessment to lead and cadmium through biological monitoring: Results of a UNEP/WHO global study. *Environ. Res.* **30,** 95–128.

Friis, L., Lars Petersson, L., and Edling, C. (1998) Reduced cadmium levels in human kidney cortex in Sweden. *Environ. Health Perspect.* **106,** 175–178.

Goyer, R. A., Epstein, S., Bhattachatyya, M., Korach, K. S., and Pounds, J. (1994). Environmental risk factors for osteoporosis. *Environ. Health Perspect.* **102,** 337–412.

Grandjean, P. (1991). Effects on reserve capacity: Significance for exposure limits. *Sci. Total Environ.* **101,** 25–32.

Grandjean, P. (1995). Individual susceptibility to toxicity. *Toxicol. Lett.* **77,** 105–108.

Hense, H-W., Filipiak, B., Novak, L., and Stoeppler, M. (1992). Nonoccupational determinants of blood lead concentrations in a general population. *Int. J. Epidemiol.* **21,** 753–762.

Hänninen, H., Hernberg, S., and Mantere, P. (1978). Psychological performance of subjects with low exposure to lead. *J. Occup. Med.* **20,** 683–689.

Järup, L., Persson, B., and Elinder, C-G. (1997). Blood cadmium—a useful indicator of dose in long term follow-up of previously cadmium exposed workers. *Scand. J. Work Environ. Health* **23,** 31–36.

Järup, L., Berglund, M., Elinder, C.-G., Nordberg, G., and Vahter, M. (1998). Health effects of cadmium exposure—a review of the literature and a risk estimate. *Scand. J. Work Environ. Health* **24,** suppl. 1, 1–52.

Jorhem, L., Mattsson, P., and Slorach, S. (1988). Lead in table wines on the Swedish market. *Food Add. Contam.* **5,** 645–649.

Jorhem, L., and Sundström, B. (1993). Levels of lead, cadmium, zinc, copper, nickel, chromium, manganese, and cobalt in foods on the Swedish market, 1983–1990. *J. Food Comp. Anal.* **6,** 223–241.

Lind, B., Vahter, M., Rahnster, B., and Björs, U. (1988). Quality control samples for the determination of lead and cadmium in blood, feces, air filters and dust. *Fresenius Z. Anal. Chem.* **332,** 741–743.

Matkovic, V. (1992). Calcium and peak bone mass. *J. Int. Med.* **231,** 151–160.

Muldoon, S. B., Cauley, J. A., Kuller, L. H., Morrow, L., Needleman, H. L., Scott, J., and Hooper, F. J. (1996). Effects of blood lead levels on cognitive function of older women. *Neuroepidemiology* **15,** 62–72.

Nilsson, U., and Skerfving, S. (1993). In vivo X-ray fluorescence measurements of cadmium and lead. *Scand. J. Work Environ. Health* **19** (Suppl. 1), 54–58.

Nordberg, G. F., and Nordberg, M. (1988). Biological monitoring of cadmium. *In* "Biological Monitoring of Toxic Metals" (T. W. Clarkson, L. Friberg, G. F. Nordberg, and P. R. Sager, Eds.), pp. 151–168. Plenum Press, New York.

Nordin, J. (1943). "Occupational Diseases," pp 133–176. Almqvist and Wiksell AB, Uppsala, Sweden.

Nunez, C. M., Klitzman, S., and Goodman, A. (1993). Lead exposure among automobile radiator repair workers and their children in New York. *Am. J. Ind. Med.* **23,** 763–777.

Passmore, R., and Eastwood, M. A. (1986). "Davidson and Passmore Human Nutrition and Dietetics," 8th Ed. Churchill Livingstone, Edinburgh.

Pedersen, N. L., Friberg, L., Floderus-Myrhed, B., McClearn, G. E., and Plomin, R. (1984). Swedish early separated twins: Identification and characterization. *Acta Genet. Med. Gemellol.* **33,** 245–250.

Pedersen, N. L., McClearn, G. E., Plomin, R., Nesselroade, J. R., Berg, S., and de Faire, U. (1991). The Swedish adoption twin study of aging: An update. *Acta Genet. Med. Gemellol.* **40,** 7–20.

Pedersen, N. L., Plomin, R., Nesselroade, J. R., and McClearn, G. E. (1992). A quantitative genetic analysis of cognitive abilities during the second half of the life span. *Psychol. Sci.* **3,** 346–353.

Rybo, E. (1985). "Diagnosis of Iron Deficiency." Doctoral thesis, pp. 1–39. University of Gothenburg. Sahlgrenska Hospital.

Silbergeld, E. K., Schwartz, J., and Mahaffey, K. (1988). Lead and osteoporosis: Mobilization of lead from bone in postmenopausal women. *Environ. Res.* **47,** 79–94.

Skerfving, S. (1993). "Inorganic Lead". Criteria documents from the Nordic expert group 1992. Nordic Council of Ministers. Arbete och Hälsa. National Institute of Occupational Health, pp. 125–238.

Skerfving, S., Nilsson, U., Schütz, A., and Gerhardsson, L. (1993). Biological monitoring of inorganic lead. *Scand. J. Work Environ. Health.* **19** (Suppl. 1), 59–64.

Staessen, J., Bernard, A., Buchet, JP., Claeys, F., Dekempeneer, L., Ducoffre, G., Fagard, R., Lauwerys, R., Lijnen, P., Roels, H., Rondia, D., Sartor, F., Thijs, L., and Amery, A. (1992). Effects of cadmium exposure on the cardiovascular system and on calcium metabolism: Results of a cross-sectional population study. *IARC Sci. Publ.* **118,** 263–269.

Staessen, J., and Lauwerys, R. (1993) Health effects of environmental exposure to cadmium in a population study. *J. Hum. Hypertens.* **7,** 195–199.

Stenlund, C. (1996). "Assessment of Occupational Exposure to Metals." Swedish Institute of Working Life, Report.

Stoeppler, M., and Brant, K. (1978). Contributions to automated trace analysis. Part II. Rapid method for the automated determination of lead in whole blood by electrothermal atomic-absorption spectrophotometry. *Analyst* **103,** 714–722.

Stoeppler, M., and Brandt, K. (1980). Contributions to automated trace analysis. Part V. Determination of cadmium in whole blood and urine by electrothermal atomic absorption spectrophotometry. *Frezenius Z. Anal. Chem.* **300,** 372–380.

Strömberg, U., Schütz, A., and Skerfving S. (1995). Substantial decrease of blood lead in Swedish children, 1978–94, associated with petrol lead. *Occup. Environ. Med.* **52,** 764–769.

Svensson, B. G., Schütz, A., Nilsson, A., and Skerfving, S. (1992). Lead exposure in indoor firing ranges. *Int. Arch. Occup. Environ. Health* **64,** 219–221.

Teitelbaum, S. L. (1993). Bone remodeling and the osteoclast. *J. Bone Min. Res.* **8** (Suppl. 2), 523–525.

Tsuritani, I., Honda, R., Ishizaki, M., Yamada, Y., and Nishijo, M. (1996). Ultrasonic assessment of calcaneus in inhabitants in a cadmium-polluted area. *J. Toxicol. Environ. Health* **48,** 131–140.

Vahter, M. (1982). "Assessment of Human Exposure to Lead and Cadmium through Biological Monitoring." Report prepared for UNEP/WHO by National Swedish Institute of Environmental Medicine and Department of Environmental Hygiene, Karolinska Institute, Stockholm. National Swedish Institute of Environmental Medicine and Karolinska Institute (Department of Environmental Hygiene), Stockholm.

Vahter, M., Berglund, M., Lind, B., Jorhem, L., Slorach, S., and Friberg, L. (1991). Personal monitoring of lead and cadmium exposure—a Swedish study with special reference to methodological aspects. *Scand. J. Work Environ. Health* **17,** 65–74.

WHO (1992). "Cadmium. Environmental Health Criteria 134." International Programme on Chemical Safety, World Health Organization, Geneva.

WHO (1995). "Inorganic Lead." *Environmental Health Criteria* 165. International Programme on Chemical Safety, World Health Organization, Geneva.

Zenz, C. (1988). "Occupational Medicine, Principals and Practical Applications," 2nd Ed., pp. 547–561. Yearbook Medical Publishers, Inc., Chicago, London, Boca Raton.